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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/610,034	07/05/00	GU	X NIH142.001C1

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EXAMINER	
SHAHNAN-SHAH, K	
ART UNIT	**PAPER NUMBER**
1645	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/610,034	Applicant(s) GU ET AL.	
	Examiner Khatol S Shahnan-Shah	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2000 and 17 July 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *11-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Applicants' Information Disclosure Statement paper # 4, received November 16, 2000 is acknowledged.

Election/Restrictions

2. Applicants' election of July 17, 2001, paper No. 9 is acknowledged.

Claims 11-34, are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected groups II-V.

3. Currently claims 1-38 are pending.

4. Claims 1-10 and 35-38 are under consideration.

Drawings

5. The drawings are objected to by the Draftsperson under 37 CFR 1.84 or 1.152. See attached form PTO 498.

Claim Objections

6. Claim 5 is objected to because of the following informalities:

Claim 5 recites the phrase " vaccine conjugate of claim 1", however claim 1 recites " a conjugate vaccine". For the purpose of consistent claim language claim 5 should also recite the phrase " conjugate vaccine of claim 1". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-10 and 35-38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition, does not reasonably provide enablement for a vaccine or a pharmaceutical composition. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to identify or make the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP) 2164.01(a). Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples (6) the quantity of experimentation, (7) the relative skill of those in the art, and (8) the breadth of the claims.

In the instant case claims 1 - 4, 8-10, and 35-38 are drawn to a vaccine. The only given example in the specification is in pages 37 and 38 mentioning that testing of the vaccine is extended to children (page 37, lines 26-30). Examiner is not sure because of the tense of the language in this section if this is prophetic or actual results or data for vaccination of individuals.

Likewise claims 5-7 are drawn to a "pharmaceutical" composition.

M.P.E.P. § 2164.01 (c), paragraph 3 recites:

When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated base on that limitation. See in re Vaeck, 947 F. 2d 488, 495,20 USPQ 2d 1438, 1444 (Fed Cir, 1991).

Steadman's Medical Dictionary (26th Edition, 1995) defines "pharmaceutical" as "relating to pharmacy or to pharmaceutics"; "pharmacy" as "the practice of preparing and dispensing drugs",

and "drug" as "Therapeutic agent; any substance, other than food, used in the prevention, diagnosis, alleviation, treatment, or cure of disease".

While the definition of "pharmaceutical" is broad, but it is not so broad to cover any use of a substance on or in the body of a subject, only those uses intend to prevent, diagnose, alleviate treat, or cure a disease within the animal to which the substance was administered.

In the instant application regarding claims 5-7 to the pharmaceutical composition, there is no working example or data given in the specification. Examiner is not sure because of the tense of the language in the specification if this is prophetic or actual results or data for the pharmaceutical composition.

Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-10 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Murphy, T.F. (U.S. Patent Numbers 5,712,118 and 5,725,862), in view of Chen, D. et al (Infection and Immunity, Vol. 64, No.6, pp. 1900-1905) and further in view of Gu et al. (U.S. Patent Number 6,207,157),

Claims 1-10 and 35-38 are drawn to a conjugate vaccine for *Moraxella catarrahlis*, comprising a detoxified lipooligosaccharide (a major surface component of *M.catarrahis*).

Murphy teaches a vaccine for *Branhamella (Moraxella) catarrahlis* from another surface component protein "CD". He teaches compositions comprising outer membrane protein " CD" and peptides and oligopeptides thereof. (see abstract Patent # 5,712,118 and claims 1 and 5 Patent # 5,725,862). Murphy does not teach the other outer membrane protein UspA (ubiquitous surface protein A).

Chen, D. et al teach evaluation of another surface component (purified UspA) from *Moraxella catarrahlis* as a vaccine in a murine model after active immunization. (see abstract).

Both Murphy and Chen do not teach LOS, which is a major surface component of most gram negative cocci, and is a possible virulence factor in the pathogenesis of infections caused by these bacteria. Major studies have been done on the LOS of *Neisseria meningitidis* (Gu et al., Infection and Immunity, Vol. 61, No. 5, pp. 1873-1880, May 1993) and *Haemophilus influenzae* (Gu et al., Infection and Immunity, Vol. 63, No. 10, pp. 4115-4120, Oct, 1995; Gu et al., Infection and Immunity, Vol. 64, No. 10, pp. 4047-4053, Oct 1996; and Gu et al., Infection and immunity, Vol. 65, No. 11, pp. 4488-4493, Nov. 1997) as potential vaccines.

Gu et al. teach a conjugate vaccine for *Haemophilus influenzae* comprising lipooligosaccharide (LOS) from which esterified fatty acids have been removed conjugated to an immunogenic carrier. The vaccine is useful for prevention of otitis media and respiratory infections in mammals (see abstract). They also teach a LOS from which esterified fatty acids have been removed from lipid A to form a detoxified LOS (dLOS), and an immunogenic carrier (a protein) covalently linked thereto (see claims 1 and 2). They further teach, wherein immunogenic carrier protein is selected from the group consisting of tetanus toxin/toxoid, a high molecular weight (HMP) isolated from nontypeable *Haemophilus influenzae*, diphtheria

toxin/toxoid, detoxified *P. aeruginosa* toxin A, cholera toxin/toxoid, pertussis toxin/toxoid and more (see claim 3). They too teach alum as an adjuvant (see claims 10-11). They also teach linker compounds such as adipic acid dihydrazide, ε- aminohexanoic acid, chlorohexanol dimethyl acetal, D- glucuronolactone and p-nitrophenylethyl amine (see claims 5-7).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of preparing a conjugate vaccine from detoxified LOS taught by Gu et al. and methods and vaccines taught by Murphy and Chen et al. to obtain the instant disclosure. Because Gu et al. teach the same method steps as the claimed invention for production of a conjugate vaccine for *Haemophilus influenzae*. One having ordinary skill in the art would have been motivated by expectation of success and the attainment of a better vaccine comprising LOS from *Moraxella catarrahlis* (which is a possible virulence factor in disease caused by this organism) and follow the same method steps to make a conjugate vaccine for prevention of *Moraxella catarrahlis* infections in humans. This will be a positive step towards prevention of disease caused by *Moraxella catarrahlis*, which has recently emerged as a significant human pathogen and may be the cause of more childhood infectious diseases than previously taught.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Khatol Shahnan-Shah whose telephone number is (703) 308-8896. The examiner can normally be reached from 7:30 AM - 4 PM on Monday through Friday. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor,

Lynette F Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned to is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

7/30/01

Khatol Shahnan-Shah, BS, Pharm, MS

Biotechnology Patent Examiner

Art Unit 1645

RODNEY P SWARTZ, PH.D
PRIMARY EXAMINER